

Spondyloarthropathy Identified as the Etiology of Nubian Erosive Arthritis

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ABSTRACT Slight variation in manifestation of different diseases may allow a single individual with one disease to mimic the “classic” appearance of another, as evidenced by the frequent confusion of spondyloarthropathy with rheumatoid arthritis. Analysis of population occurrence of arthritis (rather than isolated skeletons) facilitates more precise diagnosis.

Northeast Africans living around 2,000 years before present were clearly afflicted with a form of spondyloarthropathy. Lack of inclusion of spondyloarthropathy in the differential diagnosis of erosive arthritis led to past misclassification of Nubians as having rheumatoid arthritis. While evidence of spondyloarthropathy abounds in the literature of human skeletal disease, pre-Columbian Old World rheumatoid arthritis is still elusive. The current study further documents the absence of rheumatoid arthritis in Nubians, supporting the hypothesis that rheumatoid arthritis began in the New World. *Am J Phys Anthropol* 109:259–267, 1999. © 1999 Wiley-Liss, Inc.

Spondyloarthropathy defines a group of diseases with a tendency to reactive new (enthesial) bone formation, pauciarticular peripheral joint involvement, and frequent occurrence of axial (spine and sacroiliac) joint disease (Bywaters, 1960; Martel, 1968; McEwen et al., 1971; Ortner and Putschar, 1985; Resnick and Niwayama, 1988; Rothschild, 1982; Steinbock, 1975). Included in the spondyloarthropathy group are Reiter's syndrome (often referred to as reactive arthritis), psoriatic arthritis, ankylosing spondylitis, and the arthropathy of inflammatory bowel disease (ulcerative colitis and Crohn's disease) (McEwen et al., 1971).

In the 1950s, it was so fashionable to “lump” rheumatoid arthritis with spondyloarthropathy, that the latter received the appel-

lation “rheumatoid spondylitis” (Schilder et al., 1954; Toone et al., 1959). The recognition that these were different disorders (although sharing some characteristics) led to their separation into two categories (rheumatoid arthritis and spondyloarthropathy) (Katz, 1989; Kelly et al., 1985; McCarty, 1989; Rothschild, 1982). Unfortunately, the term rheumatoid spondylitis, and the original failure to recognize this as a separate form of arthritis, led to much diagnostic confusion in paleopathology (Bourke, 1967; Brothwell and Sandison, 1967; Duncan, 1979; Hudson et al., 1975; Klepinger, 1979; Rothschild,

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1997). The misdiagnosis by May (1898) of agonal (death-related) ulnar deviation of the hands (in a mummy) as rheumatoid arthritis is a classic illustration of the importance of great fastidiousness in assessing this question.

Although clinicians rarely have the opportunity to examine macerated bones (from individuals with validated diagnoses), clinical X-rays afford a common ground for diagnosis. Analyzing the nature and distribution of radiologic alterations allows confident confirmation of a differential diagnosis. Preliminary classification is based on alterations in bone size and configuration, presence of erosions, and evidence of reactive bone formation or remodeling (Resnick and Niwayama, 1988; Rothschild, 1982). However, bone is limited in the variety of reactions it can manifest. Perilesional, regional, or generalized increases or decreases in bony density can occur. Calcification may occur at sites of ligament, tendon, or capsule insertion. Erosions may occur solely as resorptive phenomena or may have a reactive component.

Although such options would appear to limit diagnostic ability, analyzing the alterations in light of the general skeletal distribution is more productive (Rothschild and Woods, 1989, 1991a,b; Rothschild et al., 1988; Woods and Rothschild, 1988). Isolated osseous lesions, however, are probably not attributable to specific diagnoses. It is usually not possible to accurately state that a particular disease existed in a sampled population (Bennike, 1985), based on the lesions found in a few isolated bones. Conversely, definitive diagnosis is facilitated by analysis of the "spectrum" of disease in large population samples. Expanding analysis to include radiologic appearance, pattern of involvement, nature of lesions, and association with other disease features, the manifestation of disease in a macerated skeletal population is often attributable to a specific clinical diagnosis (Rothschild and Woods, 1989, 1991a,b; Rothschild et al., 1988; Woods and Rothschild, 1988).

The report by Kilgore (1989) of erosive disease in Nubians seemed compatible with the specific diagnosis of spondyloarthropa-

thy. The latter is characterized by specific patterns of erosive joint disease and a tendency to spine and sacroiliac fusion (McEwen et al., 1971; Resnick and Niwayama, 1988; Rothschild 1982; Rothschild et al., 1994; Woodrow, 1985). The current study examines Nubian populations with special attention to especially diagnostic structures (e.g., vertebral and sacroiliac joints).

MATERIALS AND METHODS

One hundred and thirty-eight Meriotic Nubians from the Semna South Site in Northern Sudan were examined (Arizona State University, Tempe, Arizona). The site is on the west bank of the Nile River, 15 miles south (Fig. 1) of Wadi Halfa (Zabkar and Zabkar, 1982). It is dated at 2,000–1,600 years before present. While distal extremities were less well-represented in this skeletal population, axial components (e.g., vertebrae, sacroiliac joints) were preserved. Sixty-one individuals were examined from the Hassi el Abiod sites in Northern Mali (Fig. 1). Fifteen individuals were dated at 7,000 years before present (ybp), and 46 were dated at 4,500 ybp (Dutour, 1989).

Three other sites, housed at the American Museum of Natural History (New York, New York), were examined. Although skeletons from the latter sites were reasonably complete, surviving field notes are quite limited for these 19th century collections. The largest collection, designated El Hessa or the von Luschan collection, comprised 115 individuals. A second site, identified only as "near Pyramids of Light," consisted of 10 individuals, and a third site, designated "Nubian Egypt," comprised 7 individuals. These latter samples, though small in number, are included as collaborative evidence.

The skeletal remains were subjected to visual examination of all articular regions by at least two and generally three of the authors, to identify all occurrences of articular and periarticular bony alterations throughout each skeleton, to specify the types of bony alterations at each occurrence, and to map the distribution of occurrences in each skeleton. In the event of disagreement as to whether a lesion represented erosion or



Fig. 1. Map of northern Africa, noting locations of sites examined. A, Egyptian sites; B, Meriotic site; C, Hassi el Abiod.

postmortem damage, for the purpose of this study it was treated as postmortem damage.

Radiographs were selectively obtained with the bones in normal anatomic position. One author (B.M.R.) was specifically responsible for their interpretation.

RESULTS

Isolated lesions

Isolated holes, of unclear significance, were found in 10 Meriotic Nubian skeletons (7%;

affecting 1 hip, 2 knees, 4 shoulders, 1 elbow, and 2 wrists), and 5 von Luschan skeletons (4%; affecting 4 shoulders and 1 metatarsal phalangeal joint). Isolated erosions (marginal area grooves or disruptions) were found in 14 Meriotic Nubian skeletons (10%; affecting 1 hip, 7 shoulders, 3 elbows, 2 wrists, and 1 metacarpal phalangeal joint). Similar isolated erosions were found in 4 von Luschan skeletons (3%; affecting 1 shoulder, 1 wrist, 1 hip, and 1 metatarsal phalangeal joint).

TABLE 1. Frequencies of pathologic conditions¹

Site	Sample size	Spondyloarthropathy distribution										
		%	za	SI	Sho	Wrist	MCP	PIP	DIP	Ankle	MTP	DISH ²
Meriotic	138	4	6	2	1	3	1				1	18
Hassi el Abiod	61	2					1	1	1			
von Luschan	115	3	1		1	1	1	2				3
Pyramids of Light	10	10	1					1		1		
"Nubian" Egypt	7	14		1								

¹ %, frequency; za, zygapophyseal and syndesmophytes; SI, sacroiliac; Sho, shoulder; MCP, metacarpal phalangeal; PIP, proximal interphalangeal of hand; DIP, distal interphalangeal of hand; MTP, metatarsal phalangeal.

² Diffuse idiopathic skeletal hyperostosis.

Definitive lesions

Northern Sudanese spondyloarthropathy. Analysis of the Meriotic Nubian sample for axial joint involvement revealed 6 individuals (4%) with fusion of zygapophyseal joints, associated with calcification of the anulus fibrosis, resulting in syndesmophyte formation (Table 1) (Resnick and Niwayama (1988) defined syndesmophytes as "ossification within the anulus fibrosus leading to thin, vertical radiodense areas"). The thoracic spine was predominantly affected. Two instances were associated with a candle-wax-like calcification of anterior and lateral longitudinal ligaments. Vertebral involvement was an isolated phenomena in 2 individuals, associated with pauciarticular arthritis in 3 individuals, and with a monarticular (proximal humeral) hole in one other.

Peripheral joint erosions were asymmetrical in distribution and associated with exuberant, reactive perilesional new bone formation. Although hands and feet were only rarely represented in this collection, wrist fusion was noted in one individual. Erosions were marginal and subchondral in distribution, affecting that zone of metaphyseal bone within the synovial membrane and originally covered by cartilage, respectively. Radiographs revealed predominantly sclerotic perilesional margins.

Sacroiliac erosions and fusion were present in 2 individuals with vertebral involvement. One had unilateral sacroiliac involvement associated with wrist and shoulder erosions. The other had bilateral sacroiliac disease with erosions of left wrist, erosions of metacarpal phalangeal bilaterally and of the right metatarsal phalangeal joint. A hole was also present in a right distal metacarpal of that individual.

Mali spondyloarthropathy. Analysis of the Mali sample for axial joint involvement revealed one (MN27/H1) individual (2%) with asymmetrical wrist fusion and proximal interphalangeal joint subchondral erosions (Table 1). Radiographs revealed predominantly sclerotic perilesional margins.

Egyptian spondyloarthropathy. While all other observations of spine involvement were more limited in distribution, zygapophyseal joint fusion with syndesmophyte formation, simulating the appearance of a piece of bamboo, was found in one (AMNH 6575) of 10 skeletons from the site designated "near Pyramids of Light" (Table 1). The ankle and proximal interphalangeal joint erosive disease in this individual, with the "classic bamboo spine" appearance, was associated with exuberant reactive perilesional new bone formation. Sacroiliac involvement was also noted in one partial skeleton from the population labeled "Nubian Egypt."

Isolated asymmetrical proximal interphalangeal and metacarpal phalangeal joint erosive disease, associated with reactive and enthesial new bone formation, was noted in one von Luschan skeleton. Proximal interphalangeal joint fusion was noted in a second individual from that site.

Nubian infection and diffuse idiopathic skeletal hyperostosis. One infection (sternum) was noted in a Meriotic Nubian skeleton, and isolated dripping candle-wax-like calcification of the anterior longitudinal ligament (diffuse idiopathic skeletal hyperostosis) was present (Table 1) in an additional 18 (Arriaza et al., 1993). An infected hip was noted in one von Luschan skeleton, and

diffuse idiopathic skeletal hyperostosis in three.

DISCUSSION

Spondyloarthropathy

Spondyloarthropathy defines a group of diseases with a tendency to reactive new (enthesial) bone formation, pauciarticular peripheral joint involvement, and frequent occurrence of axial (spine and sacroiliac) joint disease (Arriaza, 1993; Bywaters, 1960; Martel, 1968; McEwen et al., 1971; Ortner and Putschar, 1985; Resnick and Niwayama, 1988; Rothschild, 1982; Rothschild et al., 1994; Steinbock, 1975). Zygapophyseal joint erosions and fusion appear pathognomonic for spondyloarthropathy. They have not been identified in other diseases (San Zhang and Rothschild, 1993). The classical "bamboo spine," with uniform smooth fusion of the spine, mimicking a piece of bamboo, is uncommon, although highly characteristic. Limited in occurrence to individuals with spondyloarthropathy (Katz, 1989; Kelly et al., 1985; McCarty, 1989; Resnick and Niwayama, 1988; Rothschild, 1982), it was clearly present (AMNH 6575) at the Pyramids of Light site. Northeast Africans clearly had an erosive arthropathy of the spondyloarthropathy variety.

Presence of subchondral as well as marginal erosions, characteristic of spondyloarthropathy (Rothschild and Woods, 1991a), was observed both in this study and that of Kilgore (1989). Lack of periarticular loss of bony density in this study and that of Kilgore (1989) is also characteristic of spondyloarthropathy (Bywaters, 1960; Katz, 1989; Kelly et al., 1985; McCarty, 1989; McEwen et al., 1971; Resnick and Niwayama, 1988; Rothschild, 1982; Rothschild and Woods, 1991a,b). The observed prominent remodeling of erosion margins in both studies is probably responsible for the X-ray density findings, characteristic of spondyloarthropathy (Rothschild and Woods, 1989, 1991a). "Punched out" lytic areas (holes) were also noted in these studies, often associated with bone remodeling (Rothschild and Woods, 1989, 1991a). Larger than vascularization channels (but of unclear etiology), they are common in spondyloarthropathy (Rothschild and Woods, 1989, 1991a). The erosive arthritis in

northeast (Nubian) Africa is clearly of the spondyloarthropathy variety.

The next question is, which variety? Only Reiter's syndrome and psoriatic arthritis (among the varieties of spondyloarthropathy) can occur with only limited spine involvement (yet sparing the lumbar spine) (Katz, 1989; McCarty, 1989; Rothschild, 1982). Spinal involvement in psoriatic arthritis and Reiter's syndrome can be diffuse (e.g., the "bamboo spine" noted in AMNH 7575), but tends to be more limited, as observed in this study.

As psoriatic arthritis predominantly affects the hands and Reiter's syndrome predominantly affects the feet (Resnick and Niwayama, 1988; Rothschild, 1982), it is reasonable (in view of the observed distribution of peripheral joint disease) to consider a diagnosis of psoriatic arthritis. However, Reiter's syndrome frequently complicates infectious-agent diarrhea (Colin and Fries, 1976; Katz, 1989; Leung et al., 1980; McCarty, 1989; Rothschild, 1982). In view of Old World sanitary conditions, Reiter's syndrome is also a reasonable diagnosis.

Population frequency of spondyloarthropathy in Nubian populations is fully within the range previously reported in most North American sites (Rothschild and Woods, 1992), but lower than that noted in those communities in which sanitation was compromised (Rothschild and Rothschild, 1993). Apparent exceptions at Pyramids of Light and "Nubian" Egypt sites (Table 1) reflect the small denominator and are not statistically different from the 2–4% frequencies noted at the Meriotic, Hassi el Abiod, and von Luschan sites. While Morton (1995) described disposal of personal and household waste as primitive, the frequency of spondyloarthropathy suggests that at least the water sources have not been contaminated by sewage disposal. While studies on mortality and impact of agriculture are available (Beckett and Lovell, 1994; Van Gerven et al., 1981), we were unable to find published studies directly addressing regional sanitation in the time period of interest.

Differential diagnosis

Erosive disease may complicate other forms of arthritis (other than rheumatoid

arthritis and spondyloarthropathy), but on a population basis, tends not to be common or polyarticular (Resnick and Niwayama, 1988; Rothschild, 1982).

Rheumatoid arthritis. The prominent subchondral localization of erosions in this study and that of Kilgore (1989) is at variance with observations in rheumatoid arthritis (Resnick and Niwayama, 1988; Rothschild et al., 1988, 1990, 1992a). Rheumatoid arthritis produces erosions with smooth, rounded lesional edges and excavated internal trabeculae. Lesions typically are distributed along the marginal or bare area of bone (between the area of bone covered by cartilage and the insertion of the joint capsule) as a resorptive groove or front of resorption (Leisen et al., 1987; Resnick and Niwayama, 1988; Rothschild et al., 1988, 1990). The "punched out" lesions observed in this study and by also by Kilgore (Fig. 1 in Kilgore, 1989) are quite distinct from the marginal erosions noted in rheumatoid arthritis (Rothschild et al., 1988, 1990, 1992a; Woods and Rothschild, 1988).

The reactive new bone formation in afflicted Nubians is in marked contrast to the minimal or absent perierosional bone reaction of rheumatoid arthritis. Perilesional loss of bony density (periarticular osteopenia) is uniformly present in rheumatoid arthritis (Bogoch et al., 1988; Katz, 1989; McCarty, 1989; Ropes et al., 1958; Rothschild, 1982; Rothschild et al., 1988; Woods and Rothschild, 1988). (Since a 30–50% change in bone density is required (Resnick and Niwayama, 1988) for radiologic recognition, perilesional bone reaction in rheumatoid arthritis is below that threshold.) Sclerotic reactive bone noted here and in Kilgore (1989) is notably absent at the borders of rheumatoid erosions (Bogoch et al., 1988; Katz, 1989; McCarty, 1989; Ropes et al., 1958; Rothschild, 1982; Rothschild et al., 1988; Woods and Rothschild, 1988). The perilesional bone (around the erosions) was actually increased in density in both studies, as expected in spondyloarthropathy, but incompatible with a diagnosis of rheumatoid arthritis.

Rheumatoid arthritis (on a population basis) tends to affect almost every appendicu-

lar joint, with predilection especially for carpal, ulnar styloid, metacarpophalangeal, metatarsophalangeal, and proximal interphalangeal joints. The mean number of peripheral joints involved in rheumatoid arthritis is 12 (Resnick and Niwayama, 1988; Rothschild, 1982; Rothschild and Woods, 1990). This contrasts with the limited joint involvement in Meriottic and Egyptian Nubians and only wrists, shoulders, and metacarpal phalangeal joints in the study by Kilgore (1989). Such limited erosive disease would be highly unusual in rheumatoid arthritis, but is quite characteristic of spondyloarthropathy in primates (Rothschild and Woods, 1989, 1991a,b).

The postcervical spine and sacroiliac joints are unaffected in rheumatoid arthritis. Squaring, syndesmophytes, reactive enthesial remodeling, zygapophyseal, and sacroiliac joint erosion or fusion are notably absent in rheumatoid arthritis. Ankylosis is also absent in clinical populations with rheumatoid arthritis (prior to the advent of corticosteroid therapy; see Rothschild et al., 1988, 1990; Woods and Rothschild, 1988). Presence of such phenomena in afflicted Nubians eliminates rheumatoid arthritis as a possible cause (Katz, 1989; Kelly et al., 1985; McCarty, 1989; Resnick and Niwayama, 1988; Rothschild, 1982; Rothschild et al., 1988, 1990).

As involvement is not always pauciarticular and axial joint disease is not present in all individuals with spondyloarthropathy, diagnostic confusion with rheumatoid arthritis does exist. Psoriatic arthritis (a form of spondyloarthropathy) is often a source of confusion, as 40% may have a polyarticular pattern (Moll, 1979; Rothschild and Woods, 1989). Distinguishing this form of spondyloarthropathy from rheumatoid arthritis in a single individual can be complicated, as there are five patterns of psoriatic arthritis: axial disease, distal predominant, arthritis mutilans, asymmetrical pauciarticular, and polyarticular (pseudo-rheumatoid).

Gout and infectious arthritis. Gout and infectious arthritis may produce erosions with sclerotic margins. The isolated infectious lesions identified in Nubians were clearly distinguishable from spondyloar-

thropathy. The predominantly monoarticular nature of infectious arthritis and gout (Katz, 1989; McCarty, 1989; Rothschild, 1982; Rothschild and Heathcote, 1995; Rothschild and Woods, 1990) and lack of a periosteum-based overhanging lesional edge (characteristic of gout; see Katz, 1989; McCarty, 1989; Ortner and Putschar, 1985; Rothschild, 1982) are clearly distinct from the arthritis classified as spondyloarthropathy in Nubians.

Calcium pyrophosphate deposition disease. Calcium pyrophosphate deposition disease or pseudogout causes distal metacarpal sclerosis and flattening and joint surface indentations (e.g., at the radiocarpal joint of the wrist) (Genant, 1985; Resnick and Niwayama, 1988; Rothschild, 1982; Rothschild et al., 1992b). Giant subchondral cysts and cartilaginous calcium deposition are commonly present, often as a sheet of calcium which parallels the articular surface (Markel and Hart, 1982). Hemochromatosis (an iron storage disease) and hyperparathyroidism are causes of calcium pyrophosphate deposition disease which may have a pauciarticular erosive component (Resnick and Niwayama, 1988; Rothschild, 1982; Schumacher, 1985). While hemochromatosis does indeed produce radiologic changes in the metacarpal phalangeal joints, joint space narrowing (related to loss of cartilage) is the predominant radiologic lesion. Erosions appear undescribed. The soft-tissue swelling produces a rheumatoid-like clinical appearance, but the radiograph is quite different. Chondrocalcinosis, bony overgrowth, and crumbling changes of hemochromatosis are easily distinguished from marginal erosive lesions of rheumatoid arthritis.

Osteoarthritis. Cartilage fissuring in osteoarthritis causes cartilage damage, and is occasionally referred to by physicians as erosions. That use implies changes in cartilage, not bone. Osteoarthritis (formerly referred to as degenerative joint disease or DJD) actually does not produce bone erosions (Resnick and Niwayama, 1988; Rothschild, 1982; Rothschild and Woods, 1987). While erosions or holes (disruption) may be observed in the cartilage, actual erosion of subchondral bone does not occur. The mar-

ginal area (between the cartilage-covered bone and the site of insertion of the synovial membrane into the bone) is unaffected in osteoarthritis.

Isolated erosions

The significance of the observed isolated erosions or holes is unclear. As skeletal remains reflect a lifetime of potential disease exposure, and as most are below the limits of radiologic resolution, their erosive (or hole) nature would probably not have been recognized in life. Common in populations with spondyloarthropathy (Rothschild and Woods, 1993), their significance is unclear at this time.

Diffuse idiopathic skeletal hyperostosis

The significance of diffuse idiopathic skeletal hyperostosis is as a protective phenomena, not a disease (Rothschild, 1985). It is unrelated to any other recognized skeletal disease, although the appearance can be mimicked by fluorosis and by hypervitaminosis A (Faccini and Teotia, 1974; Pennes et al., 1985; Seawright and English, 1965; Singh et al., 1962). Present in 20% of men over age 50 (Rothschild, 1985), its presence in association with spondyloarthropathy in the population studied is not surprising (Arriaza et al., 1993).

Perspectives in paleopathology

Slight variation in manifestation of different diseases may allow a single individual with one disease to mimic the "classic" appearance of another (e.g., the common confusion of spondyloarthropathy with rheumatoid arthritis; see Wells, 1962). Analysis of the population occurrence of arthritis (rather than isolated skeletons) facilitates more precise diagnosis (Rothschild and Woods, 1989, 1991a,b; Rothschild et al., 1990).

North Africans were clearly afflicted with a form of spondyloarthropathy, perhaps of the Reiter's or psoriatic variety. While evidence of spondyloarthropathy abounds in the literature of human skeletal disease (Arriaza, 1993; Kramar, 1982; Ortner and Putschar, 1985; Ruffer, 1921; Smith and Jones, 1910; Steinbock, 1975; Zorab, 1961), pre-Columbian Old World rheumatoid arthritis has proven elusive (Appelboom, 1987). The

current study further documents the absence of rheumatoid arthritis in Nubians, supporting the hypothesis of Rothschild et al. (1988) that rheumatoid arthritis began as a New World disease.

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